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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,935	12/21/2000	Timothy Raymond Hirst	9274	8699

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EXAMINER	
HINES, JANA A	
ART UNIT	PAPER NUMBER
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/674,935	HIRST ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 15, 2006 has been entered.

Amendment Entry

2. The amendments filed December 15, 2006 have been entered. Claims 38, 43, 46 and 49 have been amended. Claims 1-37 have been cancelled. Claims 38-53 are under consideration in this office action.

Withdrawal of Objections

3. The objection of claims 43, 45 and 48 has been withdrawn in view of applicants' amendments and arguments.

Response to Arguments

4. Applicant's arguments filed December 15, 2006 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. The rejection of claims 38-53 under 35 U.S.C. 112, second paragraph, is maintained for reasons already of record.

The term "enhancing" renders the claim indefinite. Applicants' assert that the term compares leukocyte mediated or immunoglobulin mediated immune response with a response observed in a mammal that did not receive EtxB. However, the claims are indefinite because the claims do not refer to any type of comparison. There is no comparison in the claim language of a mammal's enhanced mediated immune response when it received the EtxB and when it did not. Thus the metes and bounds of the phrase cannot be ascertained and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention with respect to this enhanced level of an immune response. It is suggested that he claims recite the comparison. Therefore, applicants' arguments are not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The rejection of claims 38-39, 43-45 and 49 under 35 U.S.C. 102(b) as being anticipated by Williams et al., (WO 97/02045) published January 23, 1997 is maintained for reasons already of record. The rejection is on the grounds that Williams et al., clearly teach a method for enhancing the level of a leukocyte mediated or immunoglobulin mediated immune response to a vaccine against an infectious agent in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of the *Escherichia coli* heat labile enterotoxin B subunit (EtxB), wherein the EtxB is free from whole toxin and not linked to an antigen just as required by the instant claims.

Applicants' urge that Williams does not teach a method for enhancing the level of a leukocyte mediated or immunoglobulin mediated immune response to a vaccine against an infectious agent. In response to applicant's arguments, something which is old does not become patentable upon discovery of a new property. "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342,1347,

51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). *In In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel." Id. See also MPEP § 2112.01 with regard to inherency. In this case, the body of the claims simply requires the administration to a mammal a therapeutically effective amount of the EtxB which is free from whole toxin and not linked to an antigen. Williams teach said administration, therefore Williams meets the limitations of the instant claims.

In response to applicant's argument that Williams et al., is drawn to treating autoimmune disease and does not teach protection against infectious diseases, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be inherent. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Therefore, applicants' arguments are not persuasive.

Furthermore, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the

subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."); *Abbott Labs v. Geneva Pharms., Inc.*, 182 F.3d 1315, 1319, 51 USPQ2d 1307, 1310 (Fed.Cir.1999) ("If a product that is offered for sale inherently possesses each of the limitations of the claims, then the invention is on sale, whether or not the parties to the transaction recognize that the product possesses the claimed characteristics."); *Atlas Powder Co. v. Ireco, Inc.*, 190 F.3d 1342, 1348-49 (Fed. Cir. 1999) ("Because sufficient aeration' was inherent in the prior art, it is irrelevant that the prior art did not recognize the key aspect of [the] invention.... An inherent structure, composition, or function is not necessarily known."); *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343-44, 74 USPQ2d 1398, 1406-07 (Fed. Cir. 2005) (holding that a prior art patent to an anhydrous form of a compound "inherently" anticipated the claimed hemihydrate form of the compound because practicing the process in the prior art to manufacture the anhydrous compound "inherently results in at least trace amounts of" the claimed hemihydrate even if the prior art did not discuss or recognize the hemihydrate). In this case, the administration of

EtxB which is free from the whole toxin and not linked to an antigen, inherently has the ability to enhance the level of a leukocyte mediated or immunoglobulin mediated immune response to a vaccine against an infectious agent in a mammal in need thereof; therefore applicants argument is not persuasive.

Applicants' argue that Williams does not teach that the EtxB is free from whole toxin and not linked to an antigen, However at page 1, lines 35 Williams teach that EtxB is the pure subunit of the *Escherichia coli* heat labile enterotoxin. Thus this purified subunit is clearly free from the whole toxin and not linked to an antigen. Moreover, applicants' mere statements to the contrary are not equivalent to actual data and therefore are not persuasive, in view of the evidence that the EtxB is a purified subunit.

Williams et al., teach therapeutic agents for use in the treatment of mammalian diseases wherein the basis of the invention is that the pure B-subunit of *E.coli* heat labile enterotoxin (EtxB) induces differential immune response effects on lymphocytes including activation of B and T cells. Williams et al., also teach separate administration of the therapeutic agent, which is EtxB and the antigenic determinant so as to enable separate administration of the moieties. Therefore, applicants' arguments are not persuasive since Williams et al., clearly teach a method for enhancing the level of an immune response to a vaccine against an infectious agent in a mammalian subject just as required by the instant claims.

7. The rejection of claims 38-53 under 35 U.S.C. 102(b) as being anticipated by Hazama et al., (Immunology, 1993) is maintained for reasons already of record. The

rejection is on the grounds that Hazama et al., clearly teach a method for enhancing the level of a leukocyte mediated or immunoglobulin mediated immune response to a vaccine against an infectious agent in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of the *Escherichia coli* heat labile enterotoxin B subunit (EtxB), wherein the EtxB is free from whole toxin and not linked to an antigen, however the antigen is Herpes Simplex Virus –1 (HSV-1) just as required by the instant claims.

Applicants' set forth the definition of vaccine and vaccination and argue that the terms are used as a preventive inoculation to confer immunity against a specific disease. However the claims are not drawn to administering a vaccine but administering EtxB; the claims are not drawn to providing immunity against any particular infectious disease. Rather the claims are drawn to enhancing a leukocyte mediated or immunoglobulin mediated immune response to a vaccine against an infectious agent in a mammal in need thereof, by administering EtxB, wherein the EtxB is free from whole toxin and not linked to an antigen. Thus applicants' assertions are not persuasive.

Applicants' urge that HSV glycoproteins do act as vaccines, however in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies i.e., HSV glycoproteins do act as vaccines are not recited in the rejected claims 38-39, 43-45 and 49. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus applicants' arguments are not persuasive.

Applicants' argue that Hazama shows no combination of t-gD and EtxB or t-gD alone increased protective immunity against HSV infection and point to Table 2 for support. However Table 2 is show that truncated glycoproteinD of HSV-1 co-administered with interleukin 2 (IL-2) and Table 4 shows t-gD linked EtxB. Therefore, the reliance on the teachings of Tables 2 and 4 are misplaced, since neither Table 2 nor table 4 exemplify the instantly claimed invention. Table 1 clearly shows the co-administration of an HSV-1 antigen and the EtxB is free from whole toxin and not linked to an antigen. Hazama teach mucosal and systemic antibody, i.e, immunoglobulin mediated immune response elicited by immunization, just as required by the claims. There is no requirement by the claim that t-gD alone must protect mice from viral infection, thus this argument is not persuasive.

Applicants' assert that the administration taught by Hazama et al., report a low level of increased immune response. However Hazama et al., teach an enhancement, which is all that is required of the claims. The fact that Hazama et al., disclose results, which show that other administrations resulted in higher enhanced immune levels, does not distinguish the instant claims over this art. A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use. *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). Therefore, the level of significant mucosal immune response or the failing to provide protective immunity of the HSV-1 disease, does not teach away from the instant claims. There is no requirement that the instant claimed method protect against the infectious disease. Rather the claims simply require administering to a

mammal at an effective amount of the B subunit of *E.coli* heat labile enterotoxin (EtxB) as known as LTB wherein the EtxB or LTB is free from whole toxin and not linked to an antigen wherein the administration increase the levels of B and T cell lymphocyte response. Hazama et al., teaches separate proteins and co-administration and states that tgD-LTB co administered with LTB produced a 10-fold level higher level of serum antibodies (page 648). Therefore, Hazama et al., teach all the limitations of the claims. Therefore contrary to applicants' argument, the prior art does not teach away from the instant claims, since the prior art teaches the exact same method step.

Applicants' urge that Hazama does not teach a method for enhancing the level of a leukocyte mediated or immunoglobulin mediated immune response to a vaccine against an infectious agent. In response to applicant's arguments, something which is old does not become patentable upon discovery of a new property. The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In this case, the body of the claims simply requires the administration to a mammal a therapeutically effective amount of the EtxB which is free from whole toxin and not linked to an antigen. Hazama teach said administration, therefore it meets the limitations of the instant claims.

The fact that applicant has recognized another advantage, i.e, enhancing the level of a leukocyte mediated or immunoglobulin mediated immune response to a

vaccine against an infectious agent in a mammal in need thereof, which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be inherent. Furthermore, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Therefore the fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."). In this case, the administration of EtxB which is free from the whole toxin and not linked to an antigen, inherently has the ability to enhance the level of a leukocyte mediated or immunoglobulin mediated immune response to a vaccine against an infectious agent in a mammal in need thereof; therefore applicants argument is not persuasive.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 38-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Neither the specification nor originally presented claims provides support for a method for enhancing the level of a leukocyte mediated or immunoglobulin mediated immune response to a vaccine against an infectious agent in a mammal in need thereof, comprising administering to the mammal a therapeutically effective amount of the *Escherichia coli* heat labile enterotoxin B subunit (EtxB), wherein the EtxB is free from whole toxin and not linked to an antigen, as required by the instant claims.

Applicant did not point to support in the specification for a method for enhancing the level of a leukocyte mediated immune response to a vaccine against an infectious agent. Thus, there appears to be no teaching of a method for enhancing the level of a leukocyte mediated immune response to a vaccine against an infectious agent. Applicant has pointed to figures 2,3 and 12-14 of the instant specification for support of the amendment, however it appears that the entire specification appears to fail to recite support for the newly recited method of enhancement. Figures 2 and 3 show T cell proliferation and not a generic leukocyte mediated immune response. The categories of leukocytes include granulocytes, agranulocyes, neutrophils, eosinophils, basophils, monocytes, macrophages and lymphocytes. There is no teaching of another other cell types, besides the T- and B-cells. Therefore, it appears that there is no support in the specification. Therefore, applicants must specifically point to page and line number support for the identity of a method for enhancing the level of a leukocyte mediated or immunoglobulin mediated immune response to a vaccine against an infectious agent as

recited by the amended claims. Therefore, the claims incorporate new matter and are accordingly rejected.

Conclusion

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Jeffery Siew, can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
February 26, 2007

MARK NAVARRO
PRIMARY EXAMINER